DISSERTATION ON

OUTCOME OF CHILDREN BORN TO HIV POSITIVE MOTHERS

Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

in partial fulfillment of the requirement

for the award of degree of

MD BRANCH – VII

PAEDIATRIC MEDICINE

INSTITUTE OF CHILD HEALTH AND HOSPITAL FOR CHILDREN

MADRAS MEDICAL COLLEGE

CHENNAI

MARCH 2009

CERTIFICATE

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SPECIAL ACKNOWLEDGEMENT

I express my sincere thanks to **PROF. DR. T.P.KALANITI, M.D.,** the Dean, Madras Medical College for allowing me to do this dissertation and utilize the institutional facilities.

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to **Prof. Dr. Saradha Suresh, M.D., Ph.D., F.R.C.P. (Glas)**, Professor of Pediatrics, Director and Superintendent of Institute of Child Health and Hospital for Children for permitting me to undertake this study.

I am extremely thankful to **Prof. Dr. P.Venkataraman, M.D., D.C.H.,** Professor of Pediatrics and our unit chief for his guidance, invaluable help, encouragement and support throughout this study.

I am extremely thankful to Tmt. Supriya Sahu, I.A.S., Project Director, Tamilnadu State AIDS Control Society for permitting me to under take the study.

I would like to thank to **Prof. Dr. K. Saraswathi, M.D., D.G.O.,** Professor of Obstetrics and Gynaecology, Director and Superintendent of Institute of Obstetrics and Gynaecology for allowing me to do this study.

I express my heartful gratitude to **Prof. Dr. T.L. Ratnakumari, M.D., D.C.H.**, Professor of Neonatology, Institute of Obstetrics and Gynaecology.

I would like to thank Assist. **Prof. Dr. K.Nedunchelian, M.D., D.C.H.,** for his valuable guidance enabling me to do this study.

I would also like to thank our Unit Assistant Professors, **Dr. S. Geetha, M.D., D.C.H., Dr. D. Ramamani, M.D., D.C.H., Dr. M. Umakanthan, M.D., D.C.H**. for their valuable guidance and support in doing the study.

I also thank **Dr.E.Suresh, D.C.H., Dr.Sadhana, D.G.O.** and **Dr.Kavitha, D.G.O**. of ART center for their valuable help and guidance in enabling me to do this study.

I sincerely thank all the children and their parents who have submitted themselves for this study without whom this study would not have been possible.

CONTENTS

INTRODUCTION

Acquired Immuno Deficiency Syndrome (AIDS) is one of the most feared pandemic infections of the present world, which brought out hitherto unheard infections into limelight. The World Health Organization (WHO) estimated that more than 39 million persons were living with HIV infection at the end of 2004, including 2.2 million children [1].

AIDS is caused by the Human immuno deficiency virus (HIV), which was first discovered by Robert Gallo in 1981. HIV-1 and HIV-2 are RNA viruses belonging to the family of Retroviridia of genus Lentivirus. HIV-1 is divided into three major groups namely M, O, and N and further into subtypes. Group M (Major) is divided into 9 subtypes of which subtype `C' is commonly found.

HIV-1 genome contains two copies of single stranded RNA with three major sections which are:

GAG region encoding viral core proteins namely p24, p17, p9 and p6.

- POL region encoding viral enzymes namely reverse transcriptase (p51), protease (p10) and integrase (p32).

- ENV region encoding viral envelope proteins - gp120 and gp41.

Other genes in the HIV-1 genome are tat, rev, nef, vif, vpr and vpu. It does not contain vpx segment HIV-1 is the common type in India[3]. Whereas HIV-2 is seen predominantly in sub Saharan Africa with the the following unique features:

- lower rate of vertical transmission
- possible protection against HIV-1 infection
- lower levels of plasma TNF alfa
- lower viral load
- lower level of proviral DNA in circulating lymphocytes
- Non Nucleoside Reverse Transcriptase Inhibitor resistant
- has vpx gene [2]

The following cell types are infected in HIV infection

- CD_4 T cells
- Dendritic cells
- Monocytes/macrophages
- Microglial cells
- Hofbauer cells

CD_4 is a 55 k Dalton protein responsible for helper or inducer function of the immune system. It is also expressed on the surface of monocytes / macrophages and dendritic / langerhan cells.

Co receptors for HIV-1 infection are CCR 5 (present on macrophages) & CXCR 4 (present on lymphocytes) [5]

Route Of Transmission [5]

- Mother to child transmission (MTCT)
- Blood , blood products, organ and tissue transplant.
- Intra venous drug abusers
- Sexual transmission

MTCT : Commonest mode of HIV transmission in pediatric age group. With the perinatal period being the most vulnerable period for transmission of HIV infection

The various factors influencing transmission of perinatal HIV are

- High maternal viral load
- Prolonged rupture of membranes
- Sexually transmitted diseases during pregnancy
- Preterm delivery
- Obstetric procedures like episiotomy, amniocentesis
- Vitamin A deficiency
- Breast feeding
- Mastitis.
- Oral thrush in the baby.
- Low maternal CD_4 count

The rate of perinatal HIV transmission depending on maternal viral load is as follows:

- <1000 copies/ml - Transmission rate is 0%
- 1000-10000 copies/ml - Transmission rate is 16.3%
- 10001-50000 copies/ml - Transmission rate is 21.3%
- 50001-100000 copies/ml - Transmission rate is 30.9%
- >100000 copies/ml- Transmission rate is 40.6%

Estimated risk and timing of MTCT [6] can be summarized as

- During pregnancy : 5-10%
- During labor and delivery : 10-15%
- During breast feeding : 5-20%

- Overall without breast feeding : 15-25%
- Overall with breast-feeding up to 6 months: 20-35%
- Overall with breast-feeding up to 18-24 months: 30-45%

Other body fluids such as saliva, tears, sweat and urine are not known to transmit HIV infection. Saliva contains endogenous antiviral factor, HIV specific immunoglobulins, secretory leucocyte protease inhibitor (SLPI) and submandibular gland saliva strips gp120 of the virus. Hypotonicty of oral secretions further causes lysis of HIV infected cells. Transmission by human bite is rare but can occur.

Statergies for prevention of parent to child

Transmission (PPTCT)

- Antiretroviral therapy
- Elective cesarean section when maternal viral load is more than 1000copies per ml
- Avoidance of breast feeding
- Prevention of other risk factors as given previously.

Spectrum Of HIV Infection [6]

- ***Primary HIV infection***

Mucosal dendritic cells binds the gp120 molecule of the virus and presents HIV to cells expressing CD_4 molecule. Then the virus is transported to regional lymph nodes. Intense replication of the viral genome occurs inside the cells and when it reaches critical level burst of viraemia occurs. Dissemination of the virus then occurs, 3-6 weeks after infection characterized by flu like illness with fever, arthralgia, rash and lymphadenopathy. Host immunity against the virus then temporarily suppresses the viral load to low levels and symptoms of acute viral disease disappear

- ***Chronic & Persistent infection***

Usually lasts for 8-10 years in adults. It is characterized by drop in the detectable free and cell associated virus in the blood with return of CD_4 counts to almost normal level. During this period all virologic parameters in the peripheral blood are very low. Hallmark of HIV infection is that it is never eliminated completely.

- ***Advanced HIV disease***

  There is re emergence of free virus in both peripheral blood and lymph nodes with decline in CD_4 counts and loss of function. There is emergence of faster replicating HIV. Disruption of lymphnode architecture and loss of dendritic cell network occurs with change of viral phenotype from NSI to SI (more virulent)

Mechanism of CD_4 depletion and dysfunction.

- Direct damage by the virus.
- Immune mechanism triggered.
- Synctium formation induced by virulent strains eliminates hundreds of uninfected cells.
- Nonvirologic mechanism – autoimmune, anergy, super antigens, and apoptosis.
- Destruction of lymphoid.precursors

Natural history of HIV infected (untreated) has three distinct patterns namely

- ***Rapid progressors - 15-25%.***

  They are considered to be infected in utero, the immunocompetent cells are infected before their migration from their site of origin, hence they have detectable virus within first 48hrs of life. They are symptomatic within first few months of life with a median survival of 6-9 months.

- ***Slow progressors - 60-80%***

  They are considered to be infected intrapartum. Virus is detectable after first week of life. There is slow decline of viral load with a median survival of 6 years

- ***Long term survivors - <5%***

  They are considered to be infected during breast feeding, there is minimal or no progression of the disease. They have relatively normal CD_4 count and very low viral load for longer than 8 years. They remain alive for more than 20 yrs [5].

Pediatric HIV : it is unique when compared to adult HIV in that the incubation period is shorter, there is hypergammaglobinemia with nonfunctional antibodies and B cell activation early in the course of infection. Oppurtunistic infections represent primary infection and are

more severe and rapidly progressing. CNS involvement is more common.

Clinical staging of HIV infection by WHO guidelines [6]

Each stage is characterized with the following features

Primary HIV infection

- Asymptomatic
- Acute retroviral syndrome

Clinical Stage 1

- Asymptomatic
- **Persistent generalized lymphadenopathy**

Clinical Stage 2

- Unexplained persistent hepatosplenomegaly
- Papular pruritic eruptions
- Extensive wart virus infection
- Extensive molluscum contagiosum
- Recurrent oral ulcerations
- Unexplained persistent parotid enlargement
- Linear gingival erythema
- Herpes zoster
- recurrent or chronic respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)
- Fungal nail infections

Clinical Stage 3

- Moderate unexplained malnutrition not adequately responding to standard therapy
- Unexplained persistent diarrhea (diarrhea lasting 14 days or more)
- Unexplained persistent fever (temperature above 37.5 C intermittent or continuous, for longer than one month)
- Persistent oral candidiasis (beyond first 6- 8 weeks of life)
- Oral hairy leukoplakia
- Acute necrotizing ulcerative gingivitis / periodontitis
- TB lymphadenitis
- Pulmonary tuberculosis
- Severe recurrent presumed bacterial pneumonia
- Symptomatic lymphoid interstitial pneumonitis
- Chronic HIV-associated lung disease including bronchiectasis
- Unexplained anaemia (hemoglobin < 8g/dl), neutropenia (<500/mm^3) or chronic thrombocytopenia (<50 000/ mm^3)
- HIV-associated cardiomyopathy or HIV-associated
- nephropathy (u
- nexplained)

Clinical Stage 4

- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
- Pneumocystis pneumonia
- Recurrent severe presumed bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
- Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration or visceral herpes at any site)
- Extrapulmonary tuberculosis
- Kaposi sarcoma
- Oesophageal candidiasis or candidial infection of trachea, bronchi or lungs
- Central nervous system toxoplasmosis (beyond the neonatal period)
- HIV encephalopathy
- Cytomegalovirus (CMV) infection; retinitis or CMV infection affecting another organ, with onset at age over 1 month.
- Extrapulmonary cryptococcosis including meningitis
- Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis, penicilliosis)
- Chronic cryptosporidiosis

- Chronic isosporiasis
- Disseminated non-tuberculous mycobacteria infection
- Acquired HIV-associated rectal fistula
- Cerebral or B cell non-Hodgkin lymphoma
- Progressive multifocal leukoencephalopathy.

Tests for diagnosis of HIV infection

•HIV Antibody Test

•HIV viral culture

•HIV immune complex dissociated (ICD) p24 antigen test

•HIV DNA PCR

Recommendations for HIV diagnosis in < 18 months of Age:

- Definitive diagnosis of HIV infection only by virological testing
- Confirmation of HIV infection by two positive virological tests done on separate specimens
- If a single positive virological test is to be considered diagnostic in a symptomatic infant due to resource constraints, HIV antibody testing should be done after 18 months of age to confirm the diagnosis

Clinical criteria for presumptive diagnosis of severe HIV disease in infants and children < 18 months of age

A presumptive diagnosis of severe HIV disease should be made if the infant is confirmed as HIV antibody positive

and diagnosis of any AIDS-indicator condition(s) can be made or

the infant is symptomatic with two or more of the following oral thrush, severe pneumonia and severe sepsis

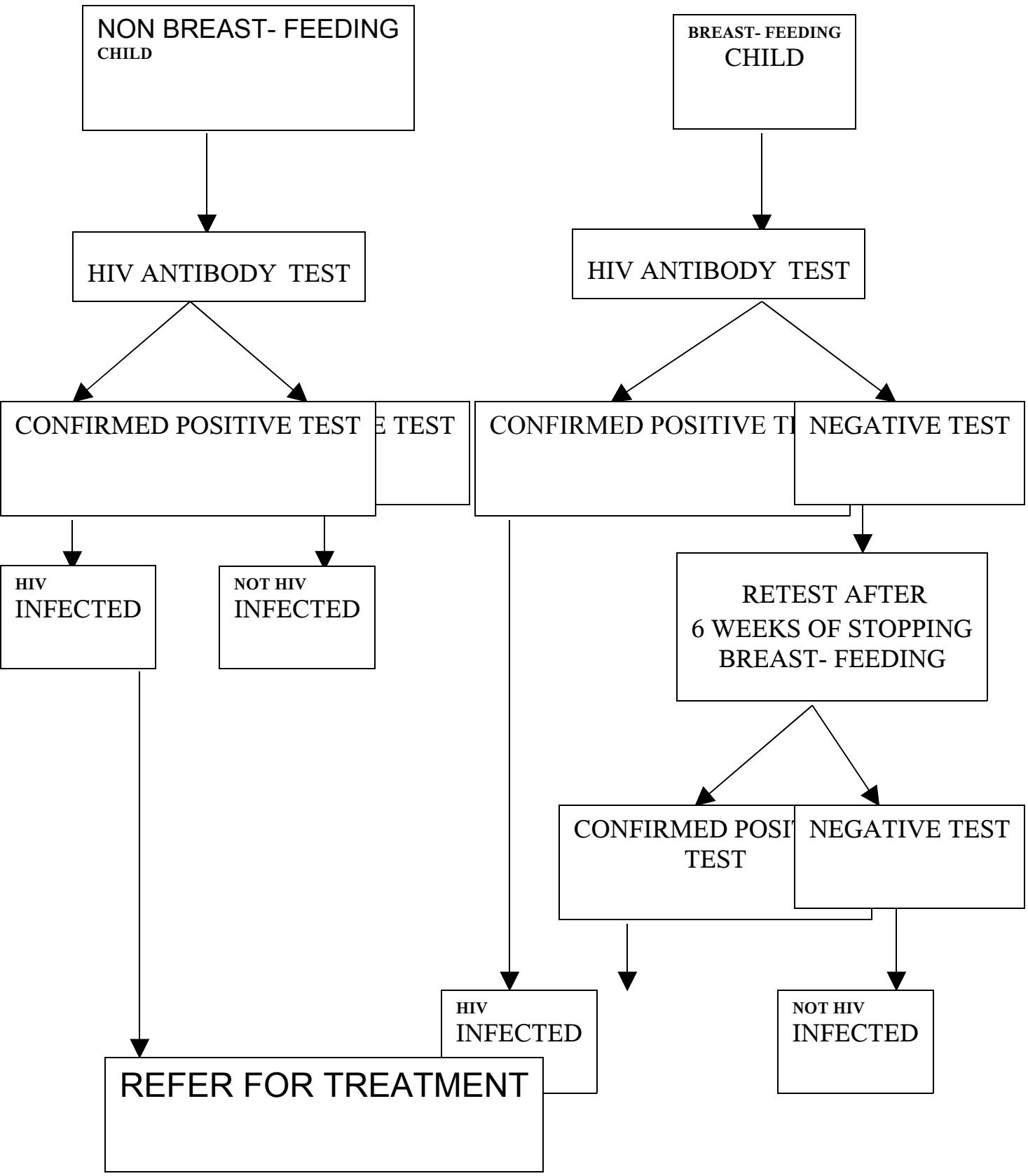
HIV Diagnosis In A Breast- Feeding Infant

- A negative virological test does not rule out HIV infection in the infant who is breast-feeding
- Virological testing should be done 6-8 weeks after complete cessation of breast-feeding
- If infant is older than 9 months at the time of stopping breast-feeding, do HIV ELISA first, if negative, no need to do virologic test
- If negative virologic test or negative HIV ELISA after 9-12 months, confirm absence of infection with a negative ELISA after 18 months

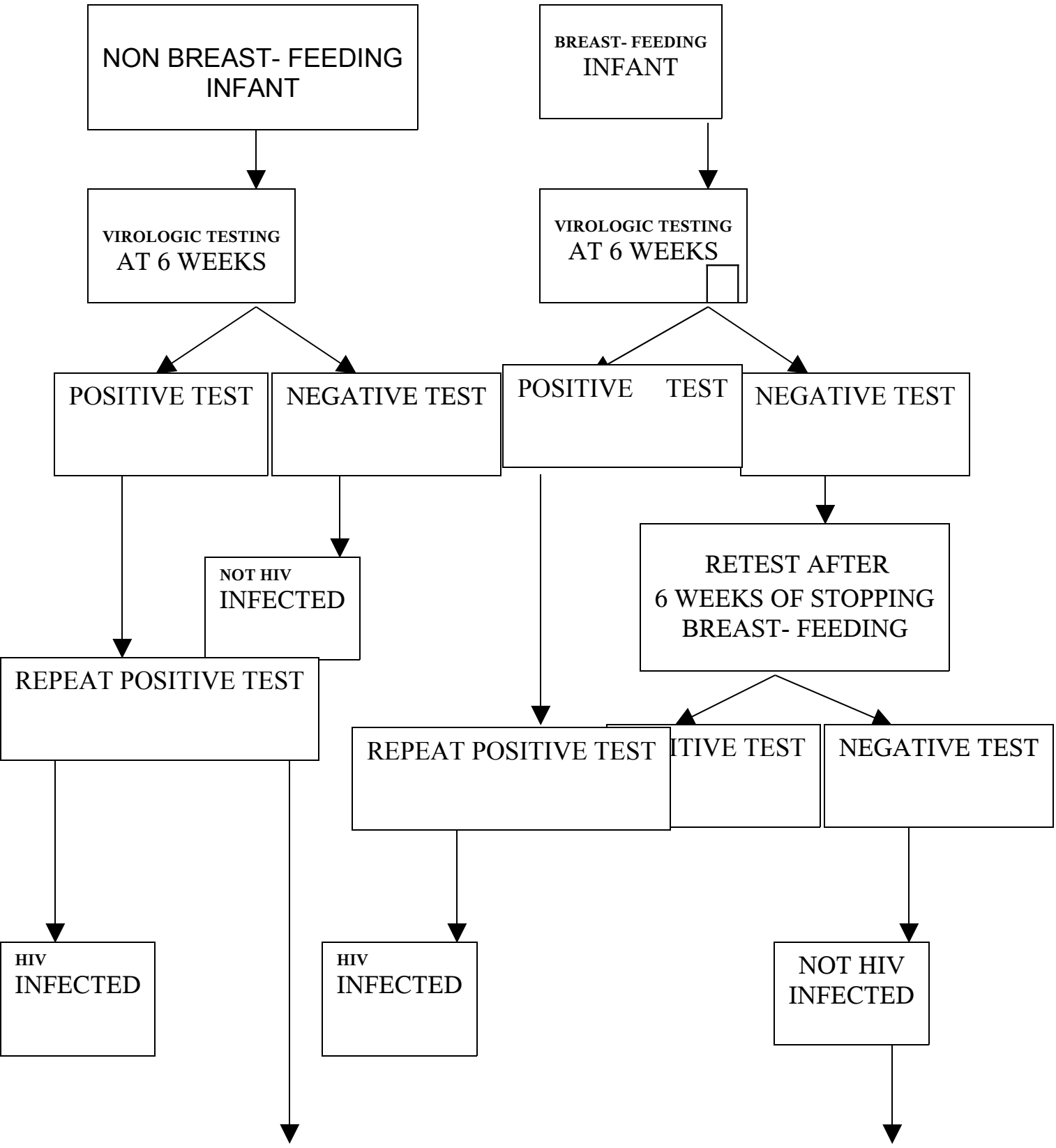
Recommendations for HIV diagnosis in > 18 months of Age:

- Definitive diagnosis using HIV antibody tests.
- A positive test should be confirmed by a second positive antibody test on the same specimen using a different assay technique.

HIV DIAGNOSIS IN > 18 MONTHS OF AGE:



FLOWHIV DIAGNOSIS IN < 18 MONTHS OF AGE:



REPEAT VIROLOGICAL TESTING IF INFANT BECOMES SYMPTOMATIC

Guidelines to start antiretroviral therapy [5]

WHO clinical stage 4 - treat all irrespective of age and CD_4 counts

WHO clinical stage 3 - <12 months of age - treat all irrespective of age and CD_4 counts.

- > 12 months of age – treat all except CD_4 guided in cases of TB, Oral hairy leukoplakia, lymphoid interstitial pneumonitis.

WHO clinical stage 1 and 2 - based on CD_4 counts.

Highly Active Antiretroviral Therapy [1]

The various classes of drugs used in the treatment of AIDS are grouped as follows:

- ***Nucleoside Reverse Transcrtiptase Inhibitors (NRTI)***

They are purine or pyrimidine analoges, which after modification in the cell (eg:- phosphorylation) selectively inhibits the viral reverse transcriptase. Thus the viral single stranded RNA is not converted to double stranded viral DNA and hence viral replication is halted.

The various drugs in this group commonly used are

Zidovudine (AZT)

Stavudine (d4t)

Didanosine (ddl)

Abacavir (ABC)

Emtricitabine (FTC)

Lamivudine (3TC)

Tenofovir (TDF)

The common adverse effects of this class of drugs are

Zidovudine - Bone marrow suppression, myopathy, hepatomegaly

Lamivudine - headache, GI intolerance

Stavudine - headache, rash, peripheral neuropathy, pancreatitis. lactic acidosis

Abacavi - Lactic acidosis, GI intolerance, hepatomegaly elevated triglycerides

- ***Non Nucleoside Reverse Transcriptase Inhibitors (NNRTI)***

These are nucleoside unrelated compounds which directly inhibit HIV–reverse transcriptase enzyme without the need for intracellular phosphorylation

The drugs in this group are

Nevirapine (NVP)

Efavirenz (EFV)

The class side effects are rash, muscle involvement and elevated liver Enzymes in addition efavirenz may produce CNS and neuropsychiatric symptoms

- ***Protease Inhibitors (PI)***

The aspartate protease enzyme encoded by HIV is involved in the production of the structural proteins and enzymes, this last step in HIV replication is inhibited by this class of drugs.

The common drugs used in this group are

Nelfinavir - (NFV)

Ritonavir - (RTV)

Lopinavir - (LPV)

Saquinavir - (SQV)

Amprenavir - (APV)

The class side effects of these drugs are hyperglycemia, hyperlipidemia, lipodystrophy, increased liver enzymes and increased bleeding disorders in hemophiliacs.

- ***Fusion Inhibitors***

This group of drugs bind to viral gp41, which prevents fusion of the virus with the CD_4 cell and hence entry of the virus into the cell. The only drug approved in this group is enfuviritide with common adverse effect of local injection site reactions.

First Line Regimen

Regimen of 2 Nucleoside Reverse Transcriptase Inhibitor plus 1 Non Nucleoside Reverse Transcriptase Inhibitor. Eg:-

Zidovudine + Lamivudine + Nevirapine or Efavirenz

Stavudine + Lamivudine + Nevirapine or Efavirenz.

Abacavir + Lamivudine + Nevirapine or Efavirenz.

Second Line Regimen

Regimen of 2 Nucleoside Reverse Transcriptase Inhibitor plus 1 Protease inhibitor (Ritonavir, Lopinavir, Nelfinavir)

LITERATURE REVIEW

Rosemary, et al from Centre Hospitalier de Kigali, Rwanda, Africa did a prospective cohort study done from November 1988 to June 1994 [8]. In the study 218 children born to HIV-1-seropositive mothers and 218 born to seronegative mothers of the same age and parity were followed up for 5yrs. Except for 4 babies of HIV positive mothers all others were breast fed upto 18 months and all were immunized upto 15 months of age.

The following conditions were regarded as HIV-related namely chronic diarrhea (>14 days), chronic cough (>14 days), chronic fever (>14 days), severe or recurrent pneumonia, hepatosplenomegaly, generalized dermatitis, lymphoid interstitial pneumonitis, oral candidiasis (beyond the neonatal period), chronic parotitis, persistent generalized lymphadenopathy (lymph nodes measuring > 0.5 cm and present in two or more extra inguinal sites), failure to thrive (< 80% of weight for age).

Of the 218 children born to HIV positive mothers, 54 were diagnosed as HIV positive. The remaining 35 children, born to seropositive mothers, had an indeterminate infection status and were excluded from the following analysis. A total of 347 children were considered uninfected, of which 138 were born to HIV-infected women and 209 to HIV-uninfected women.

Comparisions between uninfected children born to seropositive women and uninfected children born to seronegative women showed that these two groups did not differ with respect to mortality during the 5 years of follow-up (Cox hazard ratio [HR] = 0.4, 95% confidence interval [CI] = 0.1-1.6; p = 0.20).

Morbidity pattern among uninfected HIV exposed and unexposed infants were

comparable. All though severe pneumonia, generalized dermatitis and chronic parotitis were more in the HIVexposed children it was not statistically significant (p = 0.12).

The initial clinical signs that occurred most frequently in the HIV infected were failure to thrive (51.9%) and persistent lymphadenopathy (44.4%). The most frequent signs among infected children were chronic cough (97%), persistent generalized lymphadenopathy (93%), and failure to thrive (92%).

All of the HIV symptomatic conditions studied also occurred among uninfected children, although the risk of onset among uninfected children was significantly lower (3 - 13 times) than among infected children, except for chronic cough, which occurred in almost all of the children, regardless of their HIV infection status. Recurrent oral candidiasis and chronic parotitis had the greatest ability to discriminate infected from uninfected children (20 times more frequently in infected than in uninfected children).

Twenty-eight (52%) infected children and 13 (4%) uninfected children died during follow-up.

Among the 28 infected children who died, 9 met the case definition of AIDS.

The probability of death in infected children was 0.62 (95% CI: 0.47-0.78) at 5 years of age.

The estimated cumulative probability of death in uninfected children was 0.04 (95% CI: 0.02-0.07) at 5 years of age. The overall risk of death was 20.7 times higher in infected children than in uninfected children (95% CI: 10.7-40.0). Median age at death was 13.4 months for infected and 7.7 months for uninfected children). The most common causes of death among infected children were pulmonary infections (9 cases) and diarrhea (8 cases).

Increased risk of death observed in

a) an early HIV infection before 3 months of age (relative hazards of death: 10.3)

b) Short interval (< 6 months) between HIV infection and occurrence of the first HIV-related conditions (relative hazards of death: 5.4)

c) Failure to thrive as the initial pattern of clinical HIV disease ($p = 0.07$)

Decreased risk of death - chronic diarrhea, splenomegaly, or chronic parotitis (HR: 0.2, 0.3, and 0.1, respectively).

The maternal CD_4 cell count and the child's CD_4 / CD_8 ratio at 6 months of age was not predictive of death.

Of the 54 HIV infected children, 14 (26%) developed AIDS, according to the modified WHO clinical definition.

Increased risk of clinical AIDS

1) by 15 times if initial presentation was persistent generalized lymphadenopathy (95% CI: 3.1-73.9)

2) by 4.7 times if initial presentation was failure to thrive (95% CI: 1.4-16.1)

Decreased risk of developing AIDS - lymphoid interstitial pneumonitis during the course of the disease (HR: 0.04; 95% CI: 0.01-0.4)

Age at infection, interval between infection and onset of the first HIV-related conditions, and maternal and children biological characteristics were not associated with the subsequent development of clinical AIDS.

Ryder, et al from Kinshasa hospitals, Zaire.Africa did a prospective cohort study during December 1986 to April 1987 [9] which analyzed 475 infants of 466 seropositive women and the 616 infants of 606 seronegative women matched for age, parity. Of the 466 seropositive women, 85 (18%) had AIDS manifestations. The neonatal mortality among HIV exposed and unexposed were 29 (6.2%) and 8 (1.2%) respectively, $p<0.0001$. The infants of seropositive mothers, as compared with those of seronegative mothers, had lower birth weights ($p < 0.01$). Out of the 92 children with complete follow-up 36 (39%) were HIV positive. At one year, 99 (21%) infants to HIV seropositive mothers had died as compared with 23 (3.8%)born to HIV seronegative mothers ($p < 0.001$). Of the remaining surviving infants born to HIV positive mothers 29 (7.9%) had clinical AIDS.

Blanche, et al did a French collaborative study [10]. A total of 308 babies born to 308 HIV seropositive mothers were followed-up. Of the 308 mothers only one had symptoms accompanying seroconversion, all others were asymptomatic. Twelve percent of the children were delivered by cesarean section. At 18 months of age 117 children were tested for HIV, of which 32 (27%) were HIV positive. Of the 85 seronegative children, 9 (8%) had clinical signs related to HIV infection such as hepatosplenomegaly, lymphadenopathy. There was no difference in birth weight, length or head circumference between HIV infected and uninfected infants. Five of the six infants (83 %) who were breast fed were infected when compared to 25 of 99 (25%) bottle-fed infants $p < 0.01$.

Gail, et al from Bronx and Brooklyn (U.S.A) [11] has observed that HIV seropositive mothers had more sexually transmitted diseases than seronegative mothers (17.6% vs. 7.1%).

Only 3% of HIV seropositive had AIDS symptoms. Other obstetrical complications were comparable between HIV positive and negative mothers. HIV seropositive mothers had a higher rate of medical complications when compared to HIV negative mothers (43% vs. 25%). Infant factors at birth such as birth weight, gestational age, head circumference and apgar scores were similar in both HIV exposed and unexposed babies. The author concludes that HIV infection in the absence of AIDS symptoms does not appear to be associated with negative pregnancy or neonatal outcomes.

Bal Runa, et al from West Bengal [12] stated that based on the observations in PPTCT centers in West Bengal the prevalence of HIV infection among antenatal mothers was 0.11%. Maternal records of 49 such mothers were obtained of which 95.34% of mothers delivered vaginally and 88.37% of the outcomes of pregnancy were live born. Only 11 babies of the total 38 live born attended the 18 month follow- up, 2 of them were detected to be HIV positive.

Rashid, et al from Mumbai.[13] did a study with 1724 HIV positive mothers. Of them only 43.6% of mothers took Zidoviduine prophylaxis for prevention of perinatal transmission of HIV. Of the 1724 mothers, 82% delivered vaginally and 18% underwent cesarean section for obstetric reasons. Counseling regarding feeding options were given and 78% opted for artificial feeds. The mother to child HIV transmission rate was 10.1%.

Adhikari, et al from Department of Pediatrics, Nelson R Mandela school of Medicine, Durban South Africa [14] had shown that the prevalence of HIV-1 infection among women attending the King Edward Hospital, Durban South Africa was 30% in 2001. Out of the 11084 babies born to HIV positive mothers admitted in neonatal unit during the period of study, 23% were classified as low birth weight. Of the total babies 476 infants born to HIV positive mothers were followed up, their maternal HIV status were as follows.

Mothers tested antenatally - 445 (93%)

Mothers tested postnatally – 33 (7%)

Only 308 infants attended follow up clinics, out of which only 85/476babies were testsed at 15-18 months for HIV infection, the results were as follows:

Number of babies tested positive by HIV ELISA and or PCR - 24 (28%) Out of 302 infants followed up, 192 (64%) had physical sign suggestive of HIV infection such as hepaatomegaly, splenomegaly, significant lymphadenopathy, monilial infection of skin/mouth/ perineum, seborrheic dermatitis or pneumonia. Most of the infants with physical signs suggestive of HIV infection had transient signs 73 (38%) or persistent signs but resiolving within 12 months 97 (43%). Only 22 (19%) babies had persistent signs not resolved by 12 months, all of them tested positive for HIV infection at 18 months of age. Among the HIV exposed infants with persistent signs co-infectious were diagnosed in 69 (59%) which were Tuberculosis in 57 babies, CMV in 8 babies, syphilis in 2 babies and Herpes Zoster in 3 babies. Only 12 of these infants were tested HIV positive at 18 months of age. So early signs suggestive of HIV infection did not predict HIV status of an infant at 18 months of age.

Major Prospective Trials Of Anti Retroviral Therapy

To Prevent Perinatal HIV Transmission

Study	Site	Breast feeding	Arm (*n*)	Antiretroviral regimen			Trans-mission %	*p*
				Ante-partum	Intra-partum	Post-partum		
PACTG 076[15]	USA	No	A (205)	ZDV at >14 weeks	ZDV	ZDV for 6 weeks	8.3	0.00006
			B (204)	placebo	placebo	placebo	25.5	
PACTG 185[16]	USA	No	A (230)	as per primary care + HIVIG	ZDV	ZDV + HIVIG	4.1	NS
			B (224)	as per primary care + IVIG	ZDV	ZDV + IVIG	6.0	
Thai[17]	Thailand	No	A (198)	ZDV at 36 weeks	ZDV	none	9.4	0.006
			B (199)	placebo	placebo	none	18.9	
Cote d'lvoire[18]	Cote d'lvoire	Yes	A (140)	ZDV at 36 weeks	ZDV	none	15.7	0.07
			B (140)	placebo	placebo	none	24.9	
DITRAME[19]	Cote d'lvoire	Yes	A (203)	ZDV at 36 weeks	ZDV	ZDV to mother for 7 days	18.0	0.028
			B (211)	placebo	placebo	none	27.5	
PETRA[20]	South Africa	Yes	A (359)	ZDV + 3TC at ≥36 weeks	ZDV + 3TC	ZDV + 3TC to mother and child for 7 days	8.6	0.001
			B (343)	placebo	ZDV + 3TC	ZDV + 3TC to mother and child for 7 days	10.8	
			C (351)	placebo	ZDV + 3TC	placebo	17.7	0.02
			D (351)	placebo	placebo	placebo	17.2	
HIVNET[21]	Uganda	Yes	A (302)	none	ZDV	ZDV to child for 7 days	25.1	0.0006
			B (307)	none	NVP	NVP to child single dose	13.1	

ZDV - Zidovudine to mother 100 mg po five times per day.

ZDV - Zidovudine at labor - 2 mg/kg iv x 1, then 1 mg/kg iv every hour in labour.

ZDV - Zidovudine to baby - 2 mg/kg po every 6 h to child for 6 weeks beginning 8–12 h after birth.

IVIg - Immunoglobulin dose 200 mg/kg iv every 4 weeks from 20–30 weeks' gestation until delivery.

Immunoglobulin- 200 mg/kg iv to child within 12 h of birth.

3TC - Lamivudine to mother - 2 mg/kg po every 12 h.

NVP - Nevirapine to mother -200 mg po x 1 at onset of labour.

NVP - Nevirapine to baby -2 mg/kg oral suspension within 72 hrs after birth, with additional dose immediately after birth to any child whose mother did not receive the intra-partum dose or received it <1 h before delivery.

STUDY JUSTIFICATION

India along with Africa share the major burden of HIV/AIDS cases but there are only limited studies on the outcome of children born to HIV positive mothers especially in South India. The various articles have conflicting results, varying duration of study and varying PPTCT methods hence lacking uniform results. Such a study is important to know the morbidity and mortality patterns in the early years of HIV exposed children.

AIM

To Study the outcome of children born to HIV positive mothers in terms of morbidity, mortality and HIV status at follow-up up to 18 months of age.

SUBJECTS AND METHODS

METHODOLOGY

STUDY DESIGN: Cohort

STUDY PLACE

Institute of Obstetrics and Gynecology, Chennai

Institute of Child Health and Hospital for children, Chennai

STUDY PERIOD: Oct 2006 to Oct 2008

POPULATION

Study Cohort- 50 Babies born to HIV sero positive Mothers.

Control Cohort- 100 Babies born to HIV sero negative Mothers.

MANOEUVRE

The study was conducted in the Institute of Obstetrics and Gynecology, Institute of Child Health and Hospital for children, Chennai. Fifty babies born to HIV positive mothers and 100 babies born to HIV negative mothers were enrolled in the study from the post-natal ward, after obtaining consent for participation in the study. Immediately after birth the newborn were given single dose of syrup. Nevirapine 2 mg/kg per oral. Maternal details were obtained from their case records. Maternal morbidity pattern were compared between HIV positive and negative mothers. The mothers were detected as HIV positive either previously or ante-natally, they were started on HAART (highly active anti retro viral therapy) based on clinical and laboratory parameters. Comparision of various maternal parameters were done between HIV positive and negative mothers. The maternal morbidities analyzed were

Anemia – defined as hemoglobin concentration <11 gm/100ml.

PIH – defined as blood pressure more than 140/90 mmHg and proteinuria detected after 20 weeks of gestation in a previously normal woman.

GDM – defined as abnormal carbohydrate tolerance with onset or first detected during pregnancy as evidenced by abnormal glucose tolerance test.

Wasting – pre pregnancy weight and height less than 45 kg and 145 cms respectively [4]

At the onset of labor the mothers were given a single dose of tablet Nevirapine 100mg or HAART continued if already on it.. The mode of delivery was labor naturalis with minimum intervention. Cesarean section was done only for obstetric reasons such as cephalo- pelvic dispropotion, prolonged rupture of membranes, fetal distress, cord around neck, fetal malpositions and non progression of labor. If the antenatal mothers were on HAART, their newborns were given syrup. Zidovudine-2mg/kg/day in five divided doses for six weeks.

The mothers were counseled about feeding options

a) Exclusive replacement feeds

b) Exclusive breast feeding for four months, abrupt stopping and
starting replacement feeds.

At birth the neonates were evaluated, anthropometric measurements, congenital anomalies and other vital parameters were noted down. The newborns requiring care were admitted in the New born ward and necessary

management done. The birth weight and neonatal morbidity were compared between babies born to HIV positive and negative mothers, the 2 groups of babies were further referred to as

HIV exposed and unexposed babies.

Infants were categorized as adequate for gestation age (AGA) and low birth weight (LBW) [1] based on weight more than 2.5 kgs and less than 2.5 kgs respectively.

The next visit scheduled was after 6 weeks, when cotrimazole prophylaxis was started for all infants. Syrup. Cotrimoxazole was given at a dose of 5 mg/kg/day The babies were then followed up every three months and at each visit, their growth and development was monitored, feeding problems were evaluated. Treatment of common ailments, nutrition advice and management were done as required. They were also evaluated for HIV related diseases.

The infants were categorized based on weight as normal nutritional status and under nourished (under nourished defined as weight below the 3rd perrcentile of WHO growth charts)

All the babies were assessed for developmental delay using Trivandrum screening test and classified as with normal development and developmental delay. The infants with developmental delay were further evaluated by Neurologist and management carried out as suggested. Specialists opinion such as physiotherapist, audiologist were sorted as required.

The infections, illnesses and congenital anomalies were tabulated for both groups of babies and comparisions were made.

The HIV status of infants was determined by HIV RNA - PCR , and at 18 months of age by ELISA for HIV antibodies. Cotrimoxazole prophylaxis was stopped after HIV status was determined as negative.The mortality patterns in both groups were analysed.

STATISTICAL ANLYSIS

Proportions of various outcome measures were arrived at.

All the outcome variables were compared between babies born to HIV positive and negative mothers.

The various outcome variables were compared between HIV exposed and unexposed babies by using the following tests:

Chi square test and two sample binomial propotion test were used to analyse the significance of association between HIV exposure and categorize outcome measures.

Relative risk (RR) with 95% confidence interval [CI] was determined.

The mean episodes and standard deviation of illnesses were compared by using student t test and significance of differences were computed by determing the p value. A p- value of < 0.05 was considered as significant.

RESULTS

❖ ***Comparision of Birth Weight Among HIV Exposed and Unexposed Babies***

Fifty babies born to HIV positive mothers and 100 babies born to HIV seronegative mothers were followed up from birth to 18 months of age. Among the 50 HIV exposed babies, 7 (14%) were low birth weight and 43 (46%) were appropriate for gestational age when compared to 12 (12%) of low birth weight babies and 88 (88%) of appropriate for gestational age babies among HIV unexposed.

HIV exposed babies were found to be 1.17 times at risk for low birth weight when compared to HIV unexposed babies, but it did not achieve statistical significance [RR:1.17 with 95% CI = (0.52 – 2.7) and p = 0.72] [Table 1].

Table: 1 Comparision of birth weight and HIV exposure

HIV EXPOSURE STATUS	**BIRTH WEIGHT**	
	LBW n (%)	**AGA n (%)**
EXPOSED	7 (14%)	43 (86%)
UNEXPOSED	12 (12%)	88 (88%)

where AGA is appropriate for gestation age and LBW is low birth weight

❖ ***Comparision of mode of delivery among HIV exposed and unexposed babies***

Mode of delivery was compared among HIV exposed and unexposed babies and

categorized as labor naturalis (LN) or caesarean section. The results were as follows:

Of the 50 HIV exposed babies, 24 (48%) were delivered by cesarean section and 26 (52%) were delivered by labor naturalis when compared to 42 (42%) and 58 (58%) respectively among HIV unexposed.

HIV exposed babies were found to be 0.88 times delivered by cesarean section when compared to HIV unexposed babies, but it did not get statistical significance [RR:0.88 with 95% CI = (0.6 – 1.27) and p = 0.48] [Table 2].

Table: 2 Comparision of mode of delivery and HIV status of mothers

HIV EXPOSURE STATUS	**MODE OF DELIVERY**	
	CESAREAN n (%)	**LN n (%)**
EXPOSED	24 (48%)	26 (52 %)
UNEXPOSED	42 (42%)	58 (58%)

where: LN – labor naturalis.

❖ ***Comparision of neonatal morbidity among HIV exposed and unexposed***

At birth out of the 50 babies born to HIV positive mothers only 3 babies required admission. The reason were as follows:

- The first baby was born preterm of approximate gestational age of 34- 36 weeks and 2 kgs. The baby was asphyxiated at birth with a Apgar score of 2/10, 5/10 and 5/10 at 1minute, 2minutes and 5 minutes respectively. The baby was admitted in the medical newborn ward. Baby developed respiratory distress at 7 hours of life and radiological picture was that of hyaline membrane disease. Baby was conservatively managed with oxygen, intravenous fluids and antibiotics. Baby condition improved, respiratory distress settled and started on nasogastric feeds. After 10 days of stay direct breast feeds were started and baby was discharged at 14 days of life. There was no neurological sequelae at discharge.

- The second baby was born preterm of approximate gestational age of 32 – 34 weeks and 1.3 kgs. The baby had intra uterine growth retardation and was started on intra venous fluids. Investigations were normal except for low serum calcium level which was promptly treated with calcium supplements. The calcium levels repeated after 5 days were normal. Baby was hemodynamically stable through out hence gradually started on expressed breast milk feeds (as per mother's choice) and then direct breast feeds. Baby was discharged after 18 days of hospital stay with intact neurological function

- The third baby was born through meconium stained liquor and was non vigorous, baby established respiration after two cycles of bag and mask ventilation. The baby was low birth weight and developed respiratory distress. The radiological picture was that of

meconium aspiration syndrome.Baby was managed with oxygen, intra venous fluids and intra venous antibiotics. Baby improved , respiratory distress setlled and was weaned from oxygen. Baby was started on replacement feeds (as per mother's choice) and discharged after10 days.

Of the 100 babies born to HIV negative mothers , 8 required admissions, the diagnoses were as follows:

- Preterm care (PT) – 2

The first baby was born at an estimated gestational age of 32-34 weeks and 1.6 kgs. Baby was admitted in the medical newborn unit and was started on intravenous fluids and supplementary oxygen for mild respiratory distress.
The blood investigations were within normal limits and chest radiograph was also normal. Baby improved with treatment and respiratory distress settled after 3 days. Baby was started on nasogastric tube feeds and gradually weaned to direct breast feeds in the next two weeks and discharged from hospital.

The second baby was admitted as borderline preterm (estimated gestational age of 36-37 weeks) and low birth weight (1.8 kgs). Baby was given expressed breast milk and then started on direct breast feeds and discharged after 4 days of hospital stay.

- Early onset Sepsis (EOS) – 2

The two babies born to mothers with prolonged rupture of membranes (duration of rupture of membranes more than 24 hours) were admitted for evaluation of early onset sepies.

The first baby was asymptomatic, the septic screen was negative and hence discharged on day 3 of life. The second baby developed respiratory distress at 10 hours of life. The baby was investigated, chest radiolograph revealed Bronchopnemonia and septic screen was negative. The baby was given iv antibiotics for 7 days respiratory distress settled and was discharged on direct breast feeds.

- Birth asphyxia (BA) – 2

Both babies were born by cesarean section for intrapartum fetal distress (as evidenced by fetal bradycardia). The first baby was resuscitated with two cycles of Bag & Mask ventilation and admitted into medical newborn with respiratory distress. Baby had convulsions on day 1 of life which was managed with iv fluids, intravenous Phenobarbitone injection. The blood investigations and radiographic investigations were normal. The baby developed no further convulsions and general condition improved. Tube feeds were started on day 4 and the baby improved and was discharged after 8 days of stay. The second baby was also resuscitated with 2 cycles of Bag & Mask ventilation and admitted into medical newborn with respiratory distress and lethargy. The blood investigations and chest radiograph was normal. The baby improved and intravenous fluids were tapered, breast feeds established and discharged after 6 days of stay.

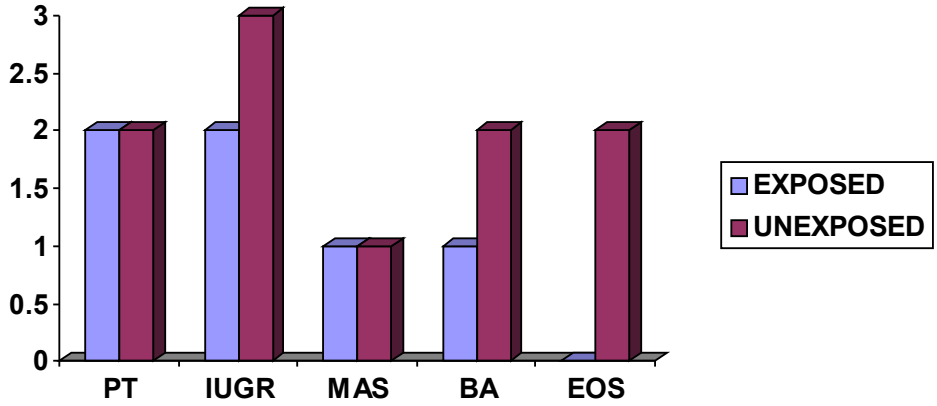
- Meconium aspiration syndrome (MAS) – 1

Baby was born by labor naturalis with meconium stained liquor. The baby was vigorous and admitted for mild respiratory distress. The respiratory distress settled by 12 hours of life, hence supplementary oxygen and intravenous fluids were stopped and breast feeds started. Baby was discharged at day 4 of life after septic screen, blood biochemistry and chest radiograph were normal.

- Intra uterine growth retardation (IUGR) – 3

All the three babies were Term / IUGR babies (birth weight was less than 1.8 kg), they were started on expressed breast feeds and investigated for metabolic abnormalities. All the investigations were normal and the babies were successfully started on direct breast feeds and discharged from hospital [Figure 1].

Figure 1 : ***Neonatal morbidities among HIV exposed and unexposed babies***



where X-axis is number of newborns.

Out of the 50 HIV exposed babies at birth 3(6%) required admission with neonatal morbidity when compared to 8(8%) of HIV exposed babies requiring admission, which was comparable between the groups (p = 0.65).

❖ ***Comparision of medical illness among HIV positive and negative mothers***

Common maternal illnesses such as anemia, pregnancy induced hypertension (PIH), gestational diabetes (GDM) and wasting were compared between HIV positive and negative mothers.

Maternal anemia was found to be more common in HIV positive mothers (82%) than in

HIV negative mothers (61%), (p = 0.009).

Similarly wasting was found to be more common in HIV positive mothers (12%) than in HIV negative mothers (1%), (p = 0.009).

Table: 3 Comparision of medical illness among HIV positive and negative mothers

MATERNAL ILLNESS	HIV STATUS		STATISTICAL SIGNIFICANCE P value
	POSITIVE n (%)	NEGATIVE n (%)	
ANEMIA	41 (82%)	61 (61%)	O.009
PIH	2 (4%)	5 (5%)	0.89
GDM	0 (0 %)	1 (1%)	0.72
WASTING	6 (12%)	1 (1%)	0.009

Among the HIV positive mothers, 2(4%) had pregnancy induced hypertension which was comparable to the 5(5%) of HIV negative mothers who had pregnancy induced hypertension, (p = 0.89).

On comparing the mothers for gestational diabetes none of the HIV positive mothers had gestational diabetes where as 1(1%) HIV negative mothers had gestational diabetes which did not have statistical significance (p = 0.72) [Table 3].

❖ ***Clinical status of HIV positive mothers:***

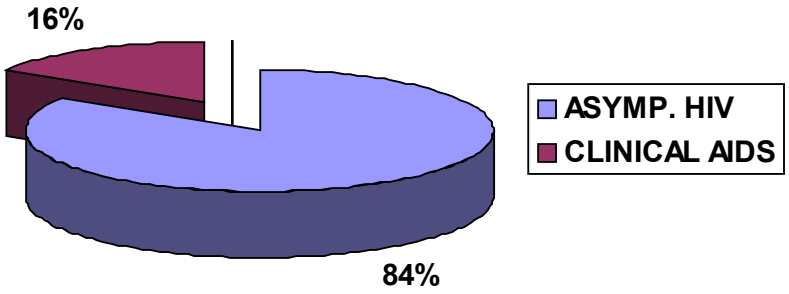
No of antenatal mothers living with HIV/AIDS – 50

No of mothers antenatally detected as HIV positive and asymptomatic –32(64%)

No of mothers previously detected and asymptomatic – 10(20%)

No of mothers with clinical AIDS and on HAART (highly active anti retroviral therapy) – 8(16%) [Figure 2].

Figure 2 : Status of HIV positive mothers



❖ ***Comparision of antiretroviral drugs used for prevention of perinatal transmission of HIV***

Total number of babies born to HIV positive mothers – 50

No. of mothers at labor and babies given single dose Nevirapine–42 (84%)

Number of babies given six weeks of Zidovudine – 8(16%)

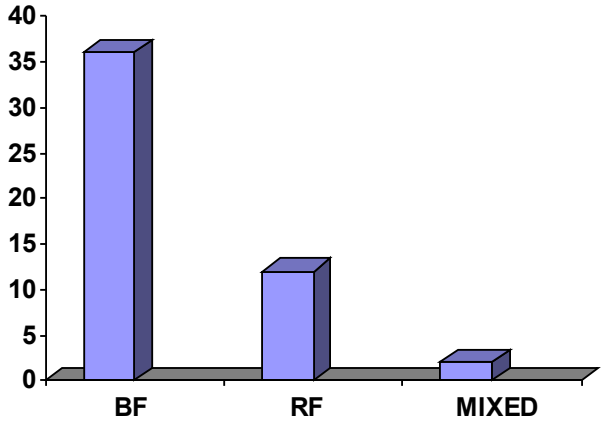
❖ ***Breast feeding options among HIV positive babies***

Among the 50 HIV positive mothers their feeding options at birth were as follows:

- Exclusive breastfeed for 4 months and then started on replacement feeds – 36(72%)
- Exclusive replacement feeds – 12(24%)
- Mixed feeding – 2(4%)

Among the HIV negative mothers only 2(2%) never breast fed [Figure 3].

Figure 3 : Feeding options among HIV positive mothers at birth:



where X-axis shows number of mothers

BF breast-feeds, RF replacement feeds, MIXED both breast-feeds and replacement feeds

Among the HIV positive women, only 2(2%) breast fed beyond 4 months of age when compared to 93(93%) of the HIV negative mothers who breast fed beyond 4 months of age.

HIV positive mothers were more likely to choose replacement feeds and shorter duration of breast-feeding, when compared to HIV negative mothers ($p = 0.001$) [Table 4].

Table: 4 Comparision of duration of breastfeeding among HIV exposed and unexposed babies

HIV EXPOSURE STATUS	DURATION OF BREAST FEEDING			
	NIL n (%)	UPTO 4 MONTHS n (%)	4 TO 6 MONTHS n (%)	MORE THAN 6 MONTHS n(%)
EXPOSED	12 (24%)	36 (72%)	2 (4%)	0 (%)
UN EXPOSED	2 (2%)	5 (5%)	23 (23%)	70 (70%)

- ***Observations on follow up: Comparision of development among HIV exposed and unexposed babies***

All the babies were assessed for developmental delay using Trivandrum screening test. Out of the 2 babies with developmental delay in HIV exposed group the first baby had perinatal asphyxia and Cerebral palsy , the second baby had seizure disorder controlled by antiepileleptic medication.

Among HIV unexposed 3 babies had developmental delay, the diagnosis of the babies were Cerebral palsy with spastic quadriparesis, global developmental delay with mental retardation and Dandy walker syndrome.

Table: 5 Comparision of development among HIV exposed and unexposed babies

HIV EXPOSURE STATUS	DEVELOPMENT	
	DELAY n(%)	NORMAL n(%)
EXPOSED	2 (4%)	48 (96%)
UN EXPOSED	3 (3%)	97 (97%)

HIV exposed babies were found to be 1.33 times at risk for developmental delay when compared to HIV unexposed babies, but it did not achieve statistical significance.

[RR: 1.33 with 95% CI = (0.52 – 2.7) and p = 0.74].

❖ ***Comparision of nutritional status among HIV exposed and unexposed babies***

Among the HIV exposed babies 5(10%) had under nutrition when compared to 9(9%) of the HIV unexposed babies. HIV exposed babies were found to be 1.1 times more at risk for under nutrition when compared to HIV unexposed babies but the difference was not statistically significant.

[RR:1.1 with 95% (CI 0.4 – 3.1) and p = 0.84] [Table 6].

Table: 6 Comparision of nutritional status among HIV exposed and unexposed babies

HIV EXPOSURE STATUS	NUTRITION	
	UNDER n(%)	NORMAL n(%)
EXPOSED	5 (10%)	45 (90%)
UN EXPOSED	9 (9%)	91 (91%)

- ***Comparision of major illness and congential anomalies among HIV exposed and unexposed babies***

Among the HIV exposed 2 babies had major illness or congenital anomalies namely seizure disorder and Cerebral palsy.

Among the HIV unexposed 5 babies had major illness or congenital anomalies namely Cerebral palsy, developmental delay, Dandy walker syndrome, lower anorectal anomaly and cleft lip.

In HIV exposed babies group 2 (4%) had major illness or congenital anomalies when compared to 5 (10%) of the HIV unexposed babies who had major illness or congenital anomalies.

HIV exposed babies were found to be 1.1 times more at risk for major illness or congenital anomalies [RR:1.1 with 95% CI (0.3 – 4) and p = 0.82] when compared to HIV unexposed babies but the difference was not statistically significant.

❖ ***Comparision of minor illnesses among HIV exposed and unexposed babies***

Table: 7 Comparision of infections among HIV exposed and un exposed babies

ILLNESS	GROUP	SAMPLE SIZE	MEAN EPISODES	STANDARD DEVIATION (S.D)	STUDENT INDEPENDANT t-TEST
URI	Exposed	50	3.58	2.977	t=1.08 P=0.28
	Unexposed	100	4.06	2.356	not significant
AWD	Exposed	50	2.28	2.214	t=3.78 P=0.001
	Unexposed	100	1.17	1.364	significant
ASOM	Exposed	50	.62	.855	t=5.08 P=0.001
	Unexposed	100	.11	.373	significant
CSOM	Exposed	50	.42	.499	t=5.68 P=0.001
	Unexposed	100	.07	.256	significant
LRI	Exposed	50	.40	.700	t=0.82 P=0.42
	Unexposed	100	.31	.598	not significant

where URI is upper respiratory tract infection, AWD is acute watery diarrhea, ASOM is acute suppurative otitis media, CSOM is chronic suppurative otitis media and LRI is lower respiratory tract infection.

The mean number of episodes of upper respiratory tract infections was 3.5 (S.D = 2.977) for HIV exposed babies when compared to 4.06 (S.D = 2.356) for HIV unexposed babies. There was no statistically significant difference in the risk of upper respiratory tract infections in HIV exposed when compared to HIV unexposed babies (p = 0.28)

The mean number of episodes of acute watery diarrhoea was 2.28 (S.D = 2.214) for HIV exposed babies when compared to 1.17 (S.D = 1.364) for HIV unexposed babies. HIV exposed

babies were 2.29 times at increased risk for developing acute watery diarrhoea when compared to HIV unexposed babies [RR: 2.29 with 95% CI = (1.15- 5.98) and p = 0.05].

The mean number of episodes of acute suppurative otitis media was 0.62 (S.D = 0.855) for HIV exposed babies when compared to 0.11 (S.D = 0.373) for HIV unexposed babies. HIV exposed babies were 7.78 times at increased risk of developing acute suppurative otitis media when compared to HIV unexposed babies [RR: 7.78 with 95% CI = (2.84-21.2) and p = 0.001].

The mean number of episodes of chronic suppurative otitis media was 0.42 (S.D = 0.499) for HIV exposed babies when compared to 0.07 (S.D = 0.256) for HIV unexposed babies. HIV exposed babies were 9.18 times at increased risk of developing chronic suppurative otitis media when compared to HIV unexposed babies [RR: 9.18 with 95% CI = (3.13-26.8) and p = 0.001].

The mean number of episodes of lower respiratory tract infections was 0.40 (S.D = 0.7) for HIV exposed babies when compared to 0.31 (S.D = 0.598) for HIV unexposed babies. There was no statistically significant difference in the risk of lower respiratory tract infections in HIV exposed when compared to HIV unexposed babies (p = 0.82)

Table: 8 Comparision of other illnesses among HIV exposed and un exposed babies

	ANEMIA n(%)	**IMPETIGO n(%)**	**WORM INFEST. n(%)**	**GEN. LN n(%)**
HIV EXPOSED	8 (16%)	4 (8%)	3 (6%)	2 (4%)
HIV UNEXPOSED	15 (15%)	7 (7%)	0 (0%)	0 (0%)

Among the HIV exposed babies, 8(16%) had anemia when compared to 15(15%) of the HIV unexposed babies. HIV exposed babies were found to be at equal risk for anemia when

compared to HIV unexposed babies

[RR:1 with 95% CI (0.5 – 2) and p = 0.83]

In HIV exposed babies group 4(8%) had impetigo when compared to 7(7%) of the HIV unexposed babies. HIV exposed babies were found to be 1.1 times more at risk for impetigo [RR:1.1 with 95% CI (0.3 – 4) and p = 0.82] when compared to HIV unexposed babies but the difference was not statistically significant

Of the 50 HIV exposed babies 3(6%) had worm infestation when compared to nil among the HIV unexposed babies. HIV exposed babies were found to be more at risk for worm infestations (p = 0.01) when compared to HIV unexposed babies. Of the 50 HIV exposed babies 2(4%) had generalized lymphadenopathy when compared to nil among the HIV unexposed babies. HIV exposed babies were found to be more at risk for worm infestations (p = 0.04) when compared to HIV unexposed babies [Table 8].

- ***Comparision of mortality rate among HIV exposed and un exposed babies***

Mortality rate at 18 months among HIV exposed babies – 2 (4%)

Mortality rate at 18 months among HIV non exposed babies – 1 (1%)

HIV exposed babies were 4 times at risk for death within 18 months of age when compared to HIV unexposed babies but it did not achieve statistical significance (p = 0.53).

Out of the 2 babies born to HIV positive mother who died within the first year:

1) The first baby was a female baby born to a primi mother by labor naturalis. Mother was a previously detected HIV patient belonging to AIDS clinical stage 4 with CD4 count 101 cells on highly active Antiretroviral therapy. She had anemia during pregnancy and

was treated with oral iron and folic acid tablets. The birth weight of the baby was 2.7 kgs and was started on Zidovudine prophylaxis for 6 weeks postnatally Mother breastfed the baby. The neonatal period was uneventful. At 40 days of life the baby presented with loose stools lasting a week on examination the baby had severe visible wasting, oral thrush, severe dehydration, generalized lymphadenopathy, and hepatospelenomegaly. The baby was treated aggressively with oxygen, intravenous fluids, intravenous antibiotics and other supportive measures. Investigations revealed bronchopneumonia in chest radiograph, blood counts showed anemia and thrombocytopenia, metabolic parameters were normal, CSF analysis was within normal limits and blood culture was awaited. HIV PCR was positive, CD4 count was 50 cells. The baby died after 26 hours of admission due to decompensated septic shock.

2) The second was a preterm (gestational age: 36 –38 week) IUGR baby delivered to a primi mother by cesarian section who was a clinical stage 3 AIDS patient with antenatal CD4 count of 200 cells. She was on highly active antiretroviral therapy. The baby was given Zidovudine prophylaxis for 6 weeks postnatally. The baby was admitted in the medical new born ward for 10 days and discharged on breastfeeds as per mothers option. The baby was given mixed feeding upto 6 weeks of life after which started on cotrimoxazole prophylaxis and stopped breast feeds as per advice. The baby was under nourished, with several episodes of diarrhoea which was managed accordingly. At five months HIV PCR was negative. At 6 months of age the baby presentated with fever, altered level of sensorium and seizures. Baby was admitted and started on anti epileptic medication, intravenous fluids, intravenous antibiotics and other supportive measures. Investigations revealed severe anemia, thrombocytosis, blood biochemical parameters were within normal limits. CSF analysis revealed polymorphonuclear leucocytosis, elevated protein, and pneumococcus in gram stain. Blood culture was negative. Baby

died after 49 hours of admission.

Lab diagnosis of HIV infection

- HIV PCR results of HIV exposed babies

Total no of HIV exposed babies screened by HIV-PCR – 50

No of HIV exposed babies with HIV PCR negative – 49

No of HIV exposed babies with HIV PCR positive – 1

- ***HIV- ELISA test results done at 18 months of age***

Total no of HIV exposed babies screened - 48

No of HIV exposed babies with HIV- ELISA negative – 48

No of HIV exposed babies with HIV ELISA positive – 0

Mother to child HIV transmission rate = 1 (2%)

DISCUSSION

India has a population of one billion, around half of whom are adults in the sexually active age group. According to WHO/UNAIDS, there are estimated 24,00,000 people living with HIV/AIDS at the end of 2007 of whom one lakh are children [7]. The average HIV prevalence among women attending antenatal clinics in India is 0.88% [7]. This emphasizes the burden of HIV in our country . Around 25% to 50% of such mothers transmit the disease to their children [6]. Number of pregnant women living with HIV/AIDS who received antiretrovirals for preventing parent to child transmission in 2007 is 8816 (which is 14% of estimated pregnant women living with HIV/AIDS) [7] depicting the need for more concentration in that area.There are very few studies especially from south India telling about impact of HIV on birth and early years of the child born to HIVpositive mothers. So our study on the outcome of children born to HIV positive mothers in terms of mortality and morbidity is important in our setup which caters to such mothers.

Our study shows that the parent to child transmission (PTCT) of HIV was only 2%. Whereas the rates were very high as quoted by Rosemary, et al from Rwanda, Africa during 1988 – 1994 of 24.7% [8], Adhikari, et al from Durban, South Africa of 28% [14], Blanche, et al from France of 27% [10]. These studies were done before the use of effective antiretrovirals for prevention of parent to child transmission of HIV. Similar studies in India by Bal Runa et al from West Bengal revealed a PTCT rate of 18.1% [12] but in that study the final number of children tested for HIV at 18 months of age was only 23% of the initial number of babies. A multicentric study HIVNET 012 revealed a PTCT rate of 13.1% [21], this low rate of PTCT in our study can be explained by the fact that the HIV seropositive mothers were evaluated for AIDS and started on combination anti retroviral therapy as per WHO guidelines. Only the

asymptomatic mothers were given single dose of nevirapine for prevention of perinatal transmission of HIV.

In our study, there was no significant difference in birth weight among HIV exposed and unexposed infants. Similar results were quoted by Gail, et al from Bronx & Brooklyn in U.S.A [11] and Blanche, et al. from France [10] But Ryder et al from Zaire, Africa has found that children born to HIV positive mothers had lower birth weights [9]. This difference would bee explained as follows, even though the percentage of mothers with AIDS were comparable between our study and that of Ryder, et al (16% vs 17.8%) [9], in our study such mothers were started on combination retroviral therapy which influenced the results.

Maternal anemia and wasting were more in HIV positive than in negative, but there was no difference in other obstetrical complications between the two groups. Similar results were obtained by Gail, et al from Bronx & Brooklyn in U.S.A [11].

In our study the rate of cesarean delivery was 48% among HIV positive which was similar to that of HIV negative mothers (42%). Whereas Rashid, et al from Mumbai, India [13]and Bal Runa, et al from West Bengal [12] has reported 18% and 4.7% respectively. These results need further large studies before being commented on.

Neonatal period was similar in both HIV exposed and unexposed babies in our study which is similar to the observations of Gail, et al from Bronx & Brooklyn in U.S.A [11. But Ryder, et al from Zaire, Africa [9] reports a higher rate of neonatal deaths among HIV exposed babies. This difference would be explained on the basis of differences in socio economic, cultural and availability of medical facilities in the different settings.

In our study only 12% of mothers opted for replacement feeds whereas Rashid, et al from Mumbai, India [13] in his study had 88% of the mothers preferring replacement feeds.

This may be due to the cultural beliefs of the people.

Our babies on follow up had similar patterns of growth and development irrespective of their maternal HIV status. This detail was not given by other studies.

In our study HIV exposed babies had an increased frequency of acute watery diarrhea and suppurative otitis media. This is contradictory to Rosemary, et al from Rwanda, Africa [8] who observed similar morbidity pattern among HIV exposed and unexposed babies in the early years. The increased frequency of acute watery diarrhea and suppurative otitis media may be due to feeding technique (gavage feeding vs breast feeding), which needs larger studies to arrive at a conclusion.

The mortality rate was not significantly more among the HIV exposed in our study, whereas Ryder et al from Zaire, Africa [9] has quoted a 6 times increased risk of death among HIV exposed babies when compared to HIV unexposed babies. This observation could be due to difference in the perinatal transmission rate of HIV and rate of symptomatic AIDS among the two studies.

SUMMARY

Thus our study on the outcome of HIV exposed babies has the following findings:

No. of HIV exposed babies studied	=	50
No. of HIV unexposed babies studied	=	100
No. of HIV exposed babies infected with HIV	=	1 (2%)

Birth characteristics and neonatal morbidity was similar in both the HIV exposed and unexposed babies.

Growth and Development was similar in HIV exposed and unexposed babies.

Acute watery diarrhea and otitis media were more common in the HIV exposed when compared to HIV unexposed babies.

Worm infestation and generalized lymphadenopathy were more common in the HIV exposed when compared to HIV unexposed babies.

There was no difference in the mortality among HIV exposed and unexposed babies.

The parent to child HIV transmission rate was 2% in our study.

CONCLUSION

Thus our study has found that HIV exposed babies are not at additional risk for neonatal adverse outcomes when compared to unexposed babies. Growth, development and major congenital anomalies are not influenced by HIV exposure. Acute watery diarrhea and otitis media are more common among HIV exposed when compared to HIV unexposed babies.

But these findings have to be confirmed by larger prospective studies.

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ANNEXURE

AT BIRTH

Mother's Name: Education : Employment :

Serial No. : HIV status : Illness :

Breast feeding option : Treatment details :

Father's Name and Address: Education : Employment :

HIV status : Illness :

Treatment details :

Baby :

Serial No. : Gestational Age : Birth Weight :

Length : Head Circumference : Apgar :

General Examination :

Congenital Anomalies :

Treatment :

FOLLOW UP

Baby Name :

Serial No :

Specific Complaints :

Weight : Head Circumference : Length:

General Examination :

Systems Examination :

Feeding : Immunisation :

Nutrition : Development :

Cotrimoxazole prophylaxis :

Other Treatment :